Complete Summary

GUIDELINE TITLE

Dementia.

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Dementia. Singapore: Singapore Ministry of Health; 2007 Mar. 80 p. [162 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Singapore Ministry of Health. Dementia. Singapore: Singapore Ministry of Health; 2001 Sep. 21 p.

The workgroup advises that these guidelines be scheduled for review 5 years after publication, or if new evidence appears that requires substantive changes to the recommendations.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- June 17, 2008, Antipsychotics (conventional and atypical]): The U.S. Food and Drug Administration (FDA) notified healthcare professionals that both conventional and atypical antipsychotics are associated with an increased risk of mortality in elderly patients treated for dementia-related psychosis. The prescribing information for all antipsychotic drugs will now include information about the increased risk of death in the BOXED WARNING and WARNING sections.
- December 12, 2007, Carbamazepine: The U.S. Food and Drug Administration (FDA) has provided recommendations for screening that should be performed on specific patient populations before starting treatment with carbamazepine.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Dementia

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management

CLINICAL SPECIALTY

Family Practice
Geriatrics
Internal Medicine
Neurology
Psychiatry

INTENDED USERS

Advanced Practice Nurses
Hospitals
Nurses
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians

GUIDELINE OBJECTIVE(S)

To provide an approach for healthcare professionals to assess, evaluate, and manage dementia (using local evidence where possible)

TARGET POPULATION

Adults with progressive cognitive or behavioural complaints suggestive of dementia, as well as patients who arouse the physician's or caregiver's suspicion of cognitive impairment despite absence of complaints

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation/Diagnosis

1. Identification of individuals with progressive cognitive or behavioural complaints suggestive of dementia, as well as those who arouse the physician's or caregiver's suspicion of cognitive impairment despite absence of complaints
2. Comprehensive evaluation including the Diagnostic and Statistical Manual of Mental Disorders – IV (DSM-IV) supplemented by an objective approach with cognitive tests; assessing the complications of dementia (behavioural and psychological symptoms, functional problems and social problems); and determining the aetiology of dementia
3. Physical examination with emphasis on detecting depression and neurological signs
4. Diagnostic tests, including full blood count, urea and serum electrolytes, serum calcium, serum glucose, thyroid function tests, vitamin B_{12} levels, and neuroimaging (computed tomography [CT], magnetic resonance imaging [MRI], positron emission tomography, or single-photon emission tomography)
5. Clinical diagnosis criteria

Management/Evaluation

1. Pharmacological management including acetylcholinesterase inhibitors (AchEI), vitamin E, and N-methyl D-aspartate (NMDA) antagonists; behavioral management (antidepressants, antipsychotics, trazodone) and follow-up assessment of response to medication and adverse events

   Note: The following medications were considered but not recommended due to lack of efficacy or insufficient data: anti-inflammatory agents, prednisolone, oestrogen, omega 3 fatty acid, folate supplementation (with or without B_{12}), ginkgo, selegiline, routine use of mood stabilizers, benzodiazepines

2. Non-pharmacological therapies such as environmental interventions; social contact; timalation (e.g., music, aromatherapy, massage); standard psychological therapies
3. Caregiver management including referral for educational programmes for caregivers, individual and family counseling, family support groups, respite care, technology-based interventions, and referral to community resources

MAJOR OUTCOMES CONSIDERED

- Utility of genetic tests
- Effectiveness of treatment:
  - Cognitive performance
  - Global function
  - Psychiatric symptoms

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

1++ High quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias

1+ Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++ High quality systematic reviews of case-control or cohort or studies
High quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+ Well conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2- Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3 Non-analytic studies e.g., case reports, case series

4 Expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guidelines have been produced by a committee of psychiatrists, neurologists, geriatricians, and primary care physicians appointed by the Ministry of Health. They were developed by the adaptation of existing guidelines, by the review of relevant literature and by expert clinical consensus with consideration of local practice.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

A. At least one meta-analysis, systematic review, or randomized controlled trial (RCT) rated as 1++, and directly applicable to the target population; or

A body of evidence, consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B. A body of evidence, including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

C. A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++

D. Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

GPP (good practice points) Recommended best practice based on the clinical experience of the guideline development group.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation is rated based on the level of the evidence and the grades of recommendation. Definitions of the grades of the recommendations (A, B, C, D, Good Practice Points [GPP]) and level of the evidence (1++ – 4) are presented at the end of the "Major Recommendations" field.

Screening and Assessment of Dementia

C - There is currently insufficient evidence for routine screening for dementia in older adults. Individuals who should be evaluated for dementia include those with progressive cognitive or behavioural complaints suggestive of dementia, as well as patients who arouse the physician's or caregiver's suspicion of cognitive impairment despite absence of complaints. (**Grade C, Level 2+**)

GPP - Assessment of dementia should be done via a comprehensive evaluation. This approach will aim to diagnose dementia early, assess for complications of dementia and establish the cause of the dementia. (**GPP**)

B - In individuals with suspected cognitive impairment, diagnosis can be made using the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria for dementia with history from a reliable informant. This can be supplemented by an objective approach with cognitive tests (Elderly Cognitive Assessment Questionnaire/Abbreviated Mental Test/Chinese Mini Mental State Examination [ECAQ/AMT/CMMSE]) and/or neuropsychological assessment. (**Grade B, Level 2++**)

B - The complications of dementia can be broadly divided into behavioural and psychological symptoms, functional problems and social problems. These should be evaluated in all patients with dementia as these issues are the major causes of stress on the caregiver and assessment would enable the clinician to target subsequent management effectively. (**Grade B, Level 2++**)

D - The aim of determining dementia aetiology is to rule out potentially reversible causes of dementia and selecting appropriate treatment strategies for the irreversible dementias. This is done via clinical history and physical examination, followed by laboratory investigations and neuroimaging (Larson et al., 1986; Clarfield, 1988; Walstra et al., 1997; Siu, 1991). (**Grade D, Level 4**)

B - A number of well-validated clinical criteria for the two most common types of dementia (Alzheimer's disease and Vascular dementia) have been developed over the years. These can be used in the specialized dementia clinics for the definition of Alzheimer's disease and vascular dementia. (**Grade B, Level 2++**)

Pharmacological Management of Dementia

GPP - Pharmacotherapy should be part of a multi-pronged strategy to dementia management that encompasses a well-established diagnosis, education of patient and caregiver, non-pharmacological measures and comprehensive caregiver psychosocial intervention. (**GPP**)

B - Although high dose vitamin E (2000 IU per day) may have a modest effect in delaying disease progression in moderately severe Alzheimer's disease, doses of vitamin E in excess of 400 IU a day should be avoided for the treatment of Alzheimer's disease until there is further data on its safety, especially in patients with cardiovascular disease. (**Grade B, Level 1+**)

A - Anti-inflammatory agents (such as non-steroidal anti-inflammatory agents and cyclo-oxygenase 2 inhibitors) are not recommended for the prevention of cognitive decline in Alzheimer's disease (Aisen et al., 2003; Reines et al., 2004). (**Grade A, Level 1++**)

B - Prednisolone is not recommended for the prevention of cognitive decline in Alzheimer's disease (Aisen et al., 2000). (**Grade B, Level 1+**)

A - Oestrogen is not recommended for the prevention of cognitive decline in women with dementia. (**Grade A, Level 1++**)

A - Acetylcholinesterase inhibitors should be considered for the management of all patients with mild to moderate Alzheimer's disease. (**Grade A, Level 1++**)

B - Acetylcholinesterase inhibitors can be considered for the management of moderate to severe Alzheimer's disease. (**Grade B, Level 1+**)

A - Acetylcholinesterase inhibitors have been shown to be of clinical benefit and may be considered for use in the management of mild to moderate vascular dementia. (**Grade A, Level 1+**)

B - Acetylcholinesterase inhibitors can be considered for the management of dementia with Lewy bodies and Parkinson's disease dementia. (**Grade B, Level 1+**)

B - All three available acetylcholinesterase inhibitors (donepezil, rivastigmine and galantamine) can be considered for the pharmacological management of dementia, since there is no definite evidence to support a difference in clinical efficacy between them. (**Grade B, Level 1+**)

A - Where tolerated, acetylcholinesterase inhibitors should be titrated to recommended doses (5 to 10 mg/day donepezil; 6 to 12 mg/day rivastigmine; 16 to 24 mg/day galantamine), which have been shown to confer greater benefit compared with lower doses. (**Grade A, Level 1++**)

B - N-methyl D-aspartate (NMDA) antagonists such as memantine can be considered for the management of moderate to severe Alzheimer's disease, either alone or in combination with acetylcholinesterase inhibitors. (**Grade B, Level 1+**)

B - N-methyl D-aspartate antagonists such as memantine may be a treatment option for mild to moderate Alzheimer's disease, if acetylcholinesterase inhibitor therapy is contra-indicated, not tolerated or if there is disease progression despite an adequate trial of acetylcholinesterase inhibitor. (**Grade B, Level 1+**)

A - N-methyl D-aspartate antagonists have been shown to be of clinical benefit and may be considered for use in the management of mild to moderate vascular dementia. (**Grade A, Level 1+**)

B - Practitioners who prescribe ginkgo for the treatment of dementia should be aware of the unestablished benefit, variability of active ingredient among preparations, and potential for drug interactions. (**Grade B, Level 1+**)

A - Selegiline is not recommended for the treatment of core or associated symptoms in Alzheimer's disease. (Birks & Flicker, 2003) (**Grade A, Level 1++**)

GPP - Appropriate treatment of vascular risk factors is recommended for all patients. However, it should be noted that whilst promising observational data exists, it remains to be shown in a randomised controlled clinical trial if any prevention strategy such as blood pressure reduction or antiplatelet treatment for the secondary prevention of stroke, will reduce the incidence of vascular dementia. (**GPP**)

GPP - The decision to initiate costly symptomatic dementia treatment, such as acetylcholinesterase inhibitors or N-methyl D-aspartate antagonists, should always be made in consultation with the patient and family after careful consideration of the expected magnitude of benefit, side effects, comorbidities and costs of treatment. (**GPP**)

GPP - Patients who are started on acetylcholinesterase inhibitors or N-methyl D-aspartate antagonists should be carefully monitored for side effects and response to treatment. (**GPP**)

Management of Behavioural and Psychological Symptoms of Dementia (BPSD)

GPP - Non-pharmacological methods to manage behavioural and psychological symptoms of dementia should be instituted, prior to consideration of pharmacological measures. (**GPP**)

GPP - Antidepressants may be used for the treatment of comorbid depression in dementia provided their use has been evaluated carefully for each patient. (**GPP**)

A - Conventional and atypical antipsychotics may be used with caution, given their side effect profile, to treat neuropsychiatric symptoms of dementia. (**Grade A, Level 1+**)

B - Trazodone may be considered for patients with depressive symptoms and dementia associated agitation. (**Grade B, Level 1+**)

A - Routine use of mood stabilizers, such as carbamazepine and sodium valproate, is not recommended for treatment of behavioural symptoms associated with dementia. (**Grade A, Level 1+**)

GPP - An individualized approach to managing behavioural problems in dementia patients is required. (**GPP**)

GPP - Cholinesterase inhibitor therapy may be considered in treatment of patients with behavioural problems if antipsychotics are inappropriate. (**GPP**)

GPP - The decision to start antipsychotic therapy to control behavioural problems in dementia patients should be made in consultation with the patient and family, after careful consideration of the benefit, adverse-effects and co-morbidities. (**GPP**)

B - For patients with dementia with Lewy Body and behavioural problems, acetylcholinesterase inhibitors should be considered first for management of the behavioural problems. (**Grade B, Level 1+**)

GPP - In all patients started on antipsychotic medication, they should be monitored carefully for side effects and response to treatment. In patients who are stable, antipsychotic withdrawal should be considered. (**GPP**)

Social and Caregiver Management of Dementia and Community Resources

A - Caregiver interventions via a multifaceted approach should be considered in the total management of the person with dementia. (**Grade A, Level 1+**)

GPP - Where appropriate, respite care can be offered to relieve the burden of caregiving on the family caregiver. (**GPP**)

GPP - Referral to community resources to meet the care needs of the person with dementia and his/her carer should always be considered. (**GPP**)

Definitions:

Levels of Evidence

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1+ Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias.

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High quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.

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4 Expert opinion.

Grades of Recommendation

A. At least one meta-analysis, systematic review, or randomized controlled trial (RCT) rated as 1++, and directly applicable to the target population; or

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Extrapolated evidence from studies rated as 1++ or 1+

C. A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++

D. Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

GPP (good practice points) Recommended best practice based on the clinical experience of the guideline development group.

CLINICAL ALGORITHM(S)

The original guideline document contains a clinical algorithm for the Management of Neuropsychiatric Symptoms of Dementia.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate assessment, evaluation, and management of patients with dementia

POTENTIAL HARMS

Adverse Effects of Medications

- Although generally well tolerated, dose-related gastrointestinal side effects (nausea, vomiting, diarrhea, anorexia) are common with *acetylcholinesterase inhibitors (AchEI)* use. These are transient and often circumvented to a large extent by a slower titration and taking the medication with food. Great caution should be exercised in those with bradycardia, sick sinus syndrome or cardiac conduction disturbances, in view of possible adverse effects of symptomatic bradycardia and syncope. Other less common side effects that have been reported include muscle cramps, insomnia, vivid dreams and weight loss. Dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD) patients commenced on AchEI should be carefully monitored for worsening of motor symptoms.
- Compared with AchEI, gastrointestinal-related side effects are uncommon with *memantine* use. Common adverse events of memantine include dizziness, headache, fatigue, hallucinations and confusion, but these tend to be transient. Memantine should be used with caution in patients with epilepsy and renal impairment, and the clinician should be aware of interactions involving commonly prescribed medications such as dextromethorphan and L-dopa.
- Doses of *vitamin E* in excess of 400 IU a day should be avoided for the treatment of Alzheimer's disease until there is further data on its safety, especially in patients with cardiovascular disease.
- Conventional antipsychotics are associated with extrapyramidal side effects and somnolence
- *Atypical antipsychotics* are associated with somnolence and gait disturbance. These adverse effects are 7.5 to 11 times more common in olanzepine-treated group compared to placebo. Serious adverse events occurred in 16.8% of risperidone versus 8.8% of placebo group, including 5 strokes and 1 transient ischaemic attacks, all in risperidone group. Meta-analysis of adverse events performed showed 3-fold statistically increased risk of cerebrovascular adverse events with risperidone and olanzepine (no statistically significant increase in mortality) while another meta-analysis comparing risk of death with atypical antipsychotics (Aripiprazole, Olanzepine, Risperidone and Quetiapine) with placebo showed increased risk of death. Other serious adverse events reported included somnolence and metabolic complications of hyperglycemia and weight gain.
- A recent retrospective cohort study had shown increased mortality among subjects using *conventional antipsychotics* compared to atypical antipsychotics. Antipsychotic medication should be used cautiously in patients

suspected to have dementia with Lewy Body as these patients have marked sensitivity to neuroleptic agents, including life-threatening neuroleptic malignant syndrome.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.
- The contents of the guideline document are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient in the light of the clinical data presented by the patient and the diagnostic and treatment options available.
- Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The following clinical audit parameters, based on recommendations in these guidelines are proposed:

1. Percentage of patients whose caregiver report subjective memory complaints underwent cognitive evaluation with subsequent appropriate management.
2. Percentage of patients newly diagnosed with dementia who had subsequent multi-pronged strategy to dementia management that encompasses education of patient and caregiver, nonpharmacological measures and comprehensive caregiver psychosocial intervention.
3. Percentage of patients newly diagnosed with dementia, institution of cognitive enhancers such as acetylcholinesterase inhibitors or N-methyl D-aspartate antagonists was made in consultation with the patient and family after careful consideration of the expected magnitude of benefit, side effects, co-morbidities and costs of treatment.
4. Percentage of patients newly diagnosed with dementia with significant behavioural problems, appropriate non-pharmacological management was instituted prior to consideration of pharmacological agents.
5. Percentage of patients newly diagnosed with dementia with significant behavioural problems despite non-pharmacological management, institution of antipsychotic therapy was made in consultation with the patient and family, after careful consideration of the benefit, adverse-effects, and co-morbidities.
6. Percentage of patients newly diagnosed with dementia who had a referral to community resources to meet the care needs of the person with dementia and his caregivers.

IMPLEMENTATION TOOLS

Clinical Algorithm
Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Dementia. Singapore: Singapore Ministry of Health; 2007 Mar. 80 p. [162 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Sep (revised 2007 Mar)

GUIDELINE DEVELOPER(S)

Singapore Ministry of Health - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

Singapore Ministry of Health

GUIDELINE COMMITTEE

Workgroup on Dementia

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Workgroup Members: Dr Chong Mei Sian (*Chairperson*) Consultant, Department of Geriatric Medicine, TTSH; Dr Christopher Chen Li-Hsian, Senior Consultant, Dept of Neurology, NNI (SGH Campus), SGH; Prof Kua Ee Heok, Head, Dept of Psychological Medicine, Yong Loo Lin School of Medicine, NUH; Dr Ng Li Ling, Senior Consultant, Dept of Psychological Medicine, CGH; Dr Lim Wee Shiong, Consultant, Dept of Geriatric Medicine, TTSH; Dr Chin Jing Jih, Consultant, Dept of Geriatric Medicine, TTSH; Dr Philip Yap Lin Kiat, Consultant, Dept of Geriatric Medicine, AH; Dr Chiam Peak Chiang, Chief & Senior Consultant, Dept of Geriatric Psychiatry, WH/IMH; Dr Francis Ngui Tet Shin, Medical Director, Adam Road Hospital; Dr Tan Kok Leong, Director, Singhealth Polyclinics-Outram

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Singapore Ministry of Health. Dementia. Singapore: Singapore Ministry of Health; 2001 Sep. 21 p.

The workgroup advises that these guidelines be scheduled for review 5 years after publication, or if new evidence appears that requires substantive changes to the recommendations.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Singapore Ministry of Health Web site.

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

AVAILABILITY OF COMPANION DOCUMENTS

The full text guideline and summary card are available for PDA download in ISilo and MSReader formats from the Singapore Ministry of Health Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on January 8, 2002. The information was verified by the guideline developer on February 22, 2002. This NGC summary was updated by ECRI Institute on July 11, 2007. This summary was updated by ECRI Institute on October 31, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs. This summary was updated by ECRI Institute on January 10, 2008, following the U.S. Food and Drug Administration advisory on

Carbamazepine. This summary was updated by ECRI Institute on July 25, 2008, following the U.S. Food and Drug Administration advisory on Antipsychotics.

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